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EXAMINER

COOK, LISA V

ART UNIT

PAPER NUMBER

1641

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

08/837,301

Applicant(s)

STEVEN ET AL.

Examiner

Lisa V. Cook

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**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 24 January 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 24 January 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: None.

Claim(s) objected to: None.

Claim(s) rejected: 57-67.

Claim(s) withdrawn from consideration: 68-97.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

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### **ADVISORY ACTION**

#### ***Amendment Entry***

1. Applicants' Request for reconsideration (Paper #20, filed 1/24/02) is acknowledged. In response to amendment-C filed therein, the specification was amended to replace page 1.

Currently, claims 57-67 are pending and under consideration.

### ***OBJECTIONS WITHDRAWN***

#### ***Specification***

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The disclosure is objected to because of the following informalities: The first page of the specification is not numbered. Appropriate correction has been received by amendment.

### ***OBJECTIONS MAINTAINED***

#### ***Drawings***

3. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948). Applicant is required to submit a proposed drawing correction in reply to this Office action. Objection is maintained.

## **INFORMATION ON HOW TO EFFECT DRAWING CHANGES**

### **A. Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

### **B. Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

### **Timing of Corrections**

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

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***Information Disclosure Statement***

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered.

***Oath/Declaration***

5. A new oath or declaration is required because:

A. Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Please see the entries for citizenship for each inventor.

B. Applicant has not given a post office address anywhere in the application papers as required by 37 CFR 1.33(a), which was in effect at the time of filing of the oath or declaration. A statement over applicant's signature providing a complete post office address is required.

C. The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 601.01(a). Please check the appropriate line.

The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. Applicant will submit a new Declaration to overcome the objections. Until receipt and consideration of the new Declaration the objection is maintained.

***REJECTIONS WITHDRAWN***

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

I. Claims 57-67 are rejected under 35 U.S.C. 102(a) as being anticipated by Ren et al. (Protein Science (1996), Vol.5, pages 1833-1843).

Ren et al. teach compositions in which molecules of interest are displayed through polymer binding. The polymers are T4 capsids and polyheads (tubular capsid variants) and the display molecules are derivatives of the dispensable capsid protein SOC. (Abstract). In figure 1, on page 1834 – the principle of the SOC display system is outlined. A surface lattice of the T4 capsid contains two dispensable proteins, SOC and HOC (claims 64 and 65). The surface lattice protein is a hexagonal array of hexamers of protein gp23\*. HOC and SOC bind to the outer surface of the gp23\* lattice: a HOC monomer binds at the center of each hexamer, and trimers of SOC bind around the trigonal sites. Peptides or polypeptides (examples with 4-residue and 316-residue peptides are shown) are expressed/displayed as C-terminal fusions of SOC and bind to the display platform. The mature surface lattice does not dissociate over a wide range of concentrations and environmental conditions. The composition is taught to be suitable in expressing an antigen (see page 1838), an enzyme see page 1839-(induce T-cell response), and an immunoglobulin (see page 1836-Immunogenicity of SOC-V3 phage). Also see page 1839-Potential application of the SOC system.

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***Response to Arguments***

Applicant argues that the cited reference lists co-inventors and is properly cited. Accordingly applicant has filed a Katz-type declaration under 37 CFR 1.132 to resolve the issue. The rejection is withdrawn.

***REJECTIONS MAINTAINED***

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 57, 62, 63, 64, 66, and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladner et al. (USP#5,403,484) in view of MacDonald et al. (Embryo Journal, 12/1984, Vol.3, No.12, pages 2863-2871)-ABSTRACT ONLY.

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Ladner et al. (USP#5,403,484) show that viruses expressing chimeric binding proteins can be useful in producing novel enzymes and hormones. (column 16, lines 1-8). Novel binding proteins against a molecule of interest encoding a protein comprising a binding domain are utilized to display a protein on the outer surface of a chosen bacterial cell, spore, or phage. See abstract.

The protein may be expressed as an insert in a chimeric bacterial outer surface protein (OSP). "All bacteria exhibit proteins on their outer surface". Column 60, lines 58-61. In order to obtain appropriate display it may be necessary to add one or more linker's amino acids between the OSP and the potential binding domain (PBD). Column 71, lines 13-22.

Ladner et al. differ from the instant invention is not specifically employing a T4 phage in the chimeric composition.

However, MacDonald et al. disclose DNA sequence and transcriptional patterns in T4 phage (*T4 surface lattice protein array*). The T4 phage is taught to be a suitable lattice protein in the instant invention. See the specification, page 2, lines 1-2 and page 12, lines 11-18. In an area between 15 and 18 kb on the standard phage T4 map, the novel gene 69 is localized. This 69 gene (*molecule of interest*) codes for two overlapping proteins that share a common C-terminal segment. The two proteins are expressed from different transcripts that are under different regulation. The smaller protein, gp69\*, can be expressed from a Escherichia coli-like promoter, but the expression of the larger protein, gp69 is delayed. The gene (69) is bracketed by DNA adenine methylase (*linker*) and the late gene SOC (*T4 dispensable polypeptide*).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the T4 phage surface lattice protein as taught by MacDonald et al. in a chimera composition as disclosed by Ladner et al. to produce outer capsid molecule display, because such T4 phage molecules as taught by MacDonald et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing T4 phage given the knowledge on its detailed structure.

One having ordinary skill in the art would have been motivated to do this because MacDonald et al. taught that the DNA sequence and transcription patterns on the standard phage T4 map is interdigitated in a complex pattern that reveals all elements that are thought to be important in regulation of the T4 gene. See abstract.

II. Claims 58, 59, 60, 61, and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ladner et al. (USP#5,403,484) in view of MacDonald et al. (Embryo Journal, 12/1984, Vol.3, No.12, pages 2863-2871)-ABSTRACT ONLY and in further view of U. Aebi et al. (J. Mol. Biol., 1977, 110, pages 687-698).

Please see discussion of Ladner et al. in view of Macdonald et al. as set forth above.

Ladner et al. in view of Macdonald et al. differ from the instant invention in failing to teach the dispensable polypeptide-HOC and the different types of molecules of interest that may be expressed in this system (antigen, enzyme, or immunoglobulin).

However, U.Aebi et al. disclose that the T4 phage has two dispensable capsids namely, soc and hoc. (page 687)

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Ladner et al., Macdonald et al., and U. Aebi et al. are all analogous art because they are from the same field of endeavor, all three inventions teach expression techniques involving phage display.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the HOC as a dispensable polypeptide and express antigens, enzymes, or immunoglobulins as specific molecules of interest as taught by U. Aebi et al. in the method of Ladner et al. in view of Macdonald et al. to perform outer capsid phage display, because such dispensable polypeptides and molecules of interest as taught by U. Aebi et al. are well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such materials, because they were already shown to be operable in the prior art.

One having ordinary skill in the art would have been motivated to do this because U. Aebi et al. taught that compositions comprising soc and hoc lattices are much more stable. See page 697, 2<sup>nd</sup> paragraph.

### ***Response to Arguments***

8. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the references do not disclose the instant invention because Ladner et al. describes molecules of interest directly fused to an OSP outer surface protein. While the instant invention teaches the linkage of the molecule of interest to a T4 dispensable polypeptide.

This argument was carefully considered but not found persuasive because a prima facie case of obviousness based on structure exists if the prior art suggests to one of ordinary skill in the art to make the substitution or modification. *In re Taborsky* (CCPA 1974) 502 F2d 775, 183 USPQ 50. Modifying the structure to link the molecule of interest with a dispensable polypeptide was shown in the prior art. Column 9, lines 13-25 in '484 discloses compositions including chimeric proteins comprising a first DNA sequence which encodes for the molecule of interest (linker) and a second DNA sequence which encodes a display means such as an outer surface protein native to the genetic package which causes the genetic package to display the chimeric protein (T4 dispensable polypeptide) on its outer surface (T4 surface lattice protein). The specific T4 phage (HOC and SOC) is further taught in the art and considered by U. Aebi et al. to be much more stable and do not adversely effect phage display.

In response to the argument that Ladner et al. only discloses compositions wherein the molecule of interest is fused directly to a coat protein and is not linked by a linker, applicant is directed to sections Column 71, lines 13-22 of U.S. Patent #5,403,484. "In order to obtain appropriate display it may be necessary to add one or more linkers amino acids between the OSP and the potential binding domain (PBD)". Also claiming an unpatentable compound in combination with a carrier/linker does not render the combination patentable if it would be obvious in the prior art to utilize a carrier/linker with the compound. *In re Lerner* (CCPA 1971) 438 F2d 1008, 169 USPQ 51; *In re Rosicky* (CCPA 1960) 276 F2d 656, 125 USPQ 341; *Ex parte Douros et al.* (POBA 1968) 163 USPQ 667 ; *In re Craige* (CCPA 1951) 189 F2d 650, 89 USPQ 609.

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In response to the argument that Ladner et al. only discloses compositions wherein the molecule of interest is fused directly to a coat protein and is not linked by a linker, applicant is directed to sections Column 71, lines 13-22 of U.S. Patent #5,403,484. "In order to obtain appropriate display it may be necessary to add one or more linkers amino acids between the OSP and the potential binding domain (PBD)".

Applicant contends that one of ordinary skill would not be motivated to link the dispensable polypeptides to another molecule via a linker and still retain the ability to bind intact phage. However, U. Aebi et al. taught that compositions comprising soc and hoc (dispensable polypeptides) and the lattices are much more stable and do not adversely effect phage display.

Given this teaching, one would be motivated to linking molecules of interest to the dispensable polypeptides in order to increase stability of the construct against dissociation and elevated temperatures while preserving the phage display capacity. See U. Aebi et al. page 697, 2<sup>nd</sup> paragraph.

9. For reasons aforementioned, no claims are allowed.

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10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
Lisa V. Cook

CM1-7B17

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2/5/02



CHRISTOPHER L. CHIN  
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